(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number: **0 460 439 A2**

(12) EUROPEAN PATENT APPLICATION

(21) Application number: **91107998.6**

(51) Int. Cl.[5]: **A61L 31/00**

(22) Date of filing: **17.05.91**

(30) Priority: **07.06.90 US 548802**

(43) Date of publication of application:
11.12.91 Bulletin 91/50

(84) Designated Contracting States:
BE CH DE DK ES FR GB GR IT LI NL SE

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(54) Deformable surgical device.

(57) A deformable surgical repair device is manufactured from either an absorbable copolymer comprising a plurality of first and second linkages or an absorbable blend of a first and second polymer. The copolymer first linkages and the first polymer in the blend are selected from the group consisting of glycolic acid ester and lactic acid ester linkages, and mixtures thereof. The copolymer second linkages and the second polymer in the blend are selected from the group consisting of 1,3-dioxan-2-one; 1,4-dioxan-2-one and ϵ-caprolactone linkages. The plurality of first linkages or the first polymer comprise at least about 50 up to about 90 mole percent of the respective copolymer or blend. The device can be combined with a reinforcing component prepared from a biocompatible polymer. The device can be further manufactured from a nonabsorbable material comprising a fluorinated hydrocarbon polymer. The device can be a fracture fixation device, or a surgical clip or staple.

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This invention relates to absorbable and partially absorbable polymeric materials possessing an enhanced ability for permanent deformation at room temperature through a crazing mechanism. This invention also relates to the use of these materials in medical device applications that require the material to be reshapable. One such application is in absorbable maxillofacial bone fixation plates where complex fracture site surface contours are often encountered. Another application is in absorbable surgical clips and staples where improved toughness and ductility are desirable.

The modification of glassy polymeric materials for improved toughness is well known in the nonabsorbable polymer prior art. Perhaps the most notable example of a toughened glassy plastic is high impact polystyrene. Many other nonabsorbable polymers have been modified for improved toughness or impact resistance. Generally, toughness and impact resistance have been improved by incorporating a discontinuous rubbery phase in the parent polymer matrix. This has been done by physical blending or by preparation of block or graft copolymers. Similar concepts have been applied to thermosets such as epoxy resins. Although increases of ductility in nonabsaorbable rubber modified plastics have been reported, the primary purpose of the modification has been to impart impact resistance and toughness. This property modification method has not been put to use in medical devices, either absorbable or nonabsorbable.

PART A DESCRIPTION

This invention relates to absorbable polymeric materials possessing an enhanced ability for permanent deformation at room temperature through a crazing mechanism. This invention also relates to the use of these materials in medical device applications that require the material to be reshapable. Applications where these materials may be useful include the following:

1. Absorbable maxillofacial bone fixation plates.
2. Absorbable bone screws or other fastening devices.
3. Absorbable surgical clips and staples.
4. Absorbable bone fixation rods and screws.

Although not specifically exemplified, it is recognized that a number of materials could be envisioned which could possess similar properties to the exemplified copolymers. To have similar properties, it is necessary that the material have a continuous "hard" phase and a "soft" phase. It is preferred that the soft phase be discontinuous, although this is not required. To form separate hard and soft phases, the hard and soft species must not be fully miscible in their final polymeric form. The final polymeric form could be a block or graft copolymer or a blend of homopolymers and/or copolymers. Alternatively, controlled blending methods could be employed with otherwise miscible polymers to minimize phase mixing in the final article. The following is a list of possible alternative materials which are included in this invention:

1. Block copolymers forming "hard" and "soft" phases.
   - A. Hard phase forming monomers
     - l. l-Lactide, d-lactide or meso-lactide
     - 2. dl-Lactide, variable ratios of d to l
     - 3. Glycolide
     - 4. Mixtures of glycolide and lactide
     - 5. Other monomers or mixtures of monomers that form absorbable polymers with glass transition temperatures above room temperature.
   - B. Soft phase forming monomers
     - 1. Trimethylene carbonate (l,3-dioxan-2-one)
     - 2. p-Dioxanone (1,4-dioxan-2-one)
     - 3. ϵ-caprolactone (2-oxepanone or oxepan-2-one)
     - 4. Mixtures of l, 2 or 3, above
     - 5. Other monomers or mixtures of monomers that form absorbable polymers with glass transition temperatures below room temperature.
2. Blends of "hard" and "soft" absorbable polymers
   - A. Hard phase forming polymers
     - 1. Poly(l-lactide), poly(d-lactide) or poly(meso-lactide)
     - 2. Copolymers of l-lactide, d-lactide or meso-lactide
     - 3. Polyglycolide
     - 4. Lactide-glycolide copolymers
     - 5. Other polymers or copolymers with glass transition temperatures above room temperature.
   - B. Soft phase forming polymers
     - 1. Poly(trimethylene carbonate)

2. Poly(p-dioxanone)
3. Poly(ϵ-caprolactone)
4. Copolymers of 1, 2, or 3, above
5. Other polymers or copolymers with glass transition temperatures below room temperature.

The selection of a preferred material will depend on the desired physical properties of the final article. The preferred material will also be determined by the desired in vivo degradation and absorption rates. Several variables can be adjusted to obtain the desired properties. Absorption rate is known to be affected by composition and crystallinity. For example a hard phase of poly(l-lactide) would provide a slow degradation rate due to its hydrophobic, crystalline nature, whereas a copolymer of glycolide and dl-lactide in equal amounts would provide a fast degradation rate due to its more hydrophilic, noncrystalline nature. If increased stiffness or strength is required, an absorbable fiber or fabric reinforcement can be added to make a composite structure. Further improvement of the composite properties can be made by manipulating the location of the reinforcement within the composite, for example, if the reinforcement is placed in the center plane of a laminated structure, the composite would be expected to be stiffer in tension (forces applied parallel to the plane) than in flexion (forces applied normal to the plane), allowing reshaping by bending.

The present invention discloses medical devices made from block copolymers. The block copolymer is composed of a lactide or a lactide/glycolide copolymer and a low glass transition temperature or a rubbery polymer such as polytrimethylene carbonate. It is the presence of the rubbery or soft block which imparts the deformability in bending to the surgical repair devices described in this application.

The following embodiments summarize the Part A inventions:

1. An article of manufacture comprising a deformable surgical repair device, the deformable surgical repair device manufactured from a copolymer, the copolymer selected from the group consisting of a block and graft copolymer, the copolymer comprising a plurality of first linkages selected from the group consisting of glycolic acid ester and lactic acid ester linkages, and mixtures thereof, and a plurality of second linkages selected from the group consisting of 1,3-dioxan-2-one; 1,4-dioxan-2-one and ϵ-caprolactone linkages, the plurality of first linkages comprising at least about 50 up to about 90 mole percent of the copolymer.

2. The article of embodiment 1 wherein the copolymer is a block copolymer.

3. The article of embodiment 2 wherein the plurality of first linkages comprises lactic acid ester linkages.

4. The article of embodiment 2 wherein the plurality of first linkages comprises glycolic acid ester linkages.

5. The article of embodiment 3 or 4 wherein the plurality of second linkages comprises 1,3-dioxan-2-one linkages.

6. An article of manufacture comprising a deformable fracture fixation device, the deformable fracture fixation device manufactured from a copolymer, the copolymer selected from the group consisting of a block and graft copolymer, the copolymer having a plurality of first linkages comprising lactic acid ester linkages and a plurality of second linkages selected from the group consisting of 1,3-dioxan-2-one and 1,4-dioxan-2-one linkages, the plurality of lactic acid ester linkages comprising more than 50 to about 80 weight percent of the copolymer.

7. The article of embodiment 6 wherein the copolymer is a block copolymer.

8. The article of embodiment 7 wherein the plurality of lactic acid ester linkages comprises about 80 weight percent of the copolymer.

9. The article of embodiment 8 wherein the plurality of second linkages comprises 1,3-dioxan-2-one linkages.

10. An article of manufacture comprising a deformable surgical repair device, the deformable surgical repair device manufactured from a blend of a first and a second absorbable polymer, the first absorbable polymer comprising a plurality of linkages selected from the group consisting of glycolic acid ester and lactic acid ester linkages, and mixtures thereof, and the second absorbable polymer comprising a plurality of linkages selected from the group consisting of 1,3-dioxan-2-one; 1,4-dioxan-2-one and ϵ-caprolactone linkages, the first absorbable polymer comprising at least about 50 up to about 90 weight percent of the blend.

11. The article of embodiment 10 wherein the first absorbable polymer is a homopolymer.

12. The article of embodiment 11 wherein the first absorbable homopolymer consists essentially of lactic acid ester linkages.

13. The article of embodiment 10 wherein the first absorbable polymer is a copolymer.

14. The article of embodiment 12 wherein the second absorbable polymer comprises a plurality of linkages selected from the group consisting of 1,3-dioxan-2-one and 1,4-dioxan-2-one linkages.

15. The article of embodiments 1, 2, 3, 10, 11, 12 or 14 wherein the deformable surgical repair device is a fracture fixation device.

16. The article of embodiment 15 wherein the fracture fixation device is a bone plate.

17. The article of embodiments 1, 2, 3, 10, 11, 12 or 14 wherein the deformable surgical repair device is a clip.

18. The article of embodiments 1, 2, 3, 10, 11, 12 or 14 wherein the deformable surgical repair device is a staple.

19. A surgical composite structure for mammalian tissue comprising:

a) a reinforcing component prepared from a plurality of fibers, plurality of the fibers manufactured from a biocompatible polymer, and

b) a bioabsorbable component comprising a copolymer

the copolymer selected from the group consisting of a block and graft copolymer, the copolymer comprising a plurality of first linkages selected from the group consisting of glycolic acid ester and lactic acid ester linkages, and mixtures thereof, and a plurality of second linkages selected from the group consisting of 1,3-dioxan-2-one; 1,4-dioxan-2-one and ϵ-caprolactone linkages, the plurality of first linkages comprising at least about 50 up to about 90 mole percent of the copolymer.

20. The structure of embodiment 19 wherein the reinforcing component is manufactured from an absorbable biocompatible polymer.

21. The structure of embodiment 20 wherein the absorbable biocompatible polymer is selected from the group consisting of a homopolymer or copolymer of polyglycolic acid, polylactic acid, polyhydroxy butyrate and blends of the same, and poly(d-lactic acid) blended with poly(l-lactic acid).

22. The structure of embodiment 19 wherein the reinforcing component is manufactured from a nonabsorbable biocompatible polymer.

23. The structure of embodiment 22 wherein the nonabosrbable biocompatible polymer is selected from the group consisting of polyethylene terephthalate, silk, nylon, polypropylene, polyethylene and polyoxymethylene and blends of the same.

24. The structure of embodiment 19, 20, 21, 22 or 23 wherein the bioabsorbable component comprises a block copolymer.

25. The structure of embodiment 24 wherein the plurality of first linkages in the block copolymer comprises lactic acid ester linkages.

26. The structure of embodiment 24 wherein the plurality of first linkages in the block copolymer comprises glycolic acid ester linkages.

27. The structure of embodiment 25 or 26 wherein the plurality of second linkages in the block copolymer comprises 1,3-dioxan-2-one linkages.

28. A surgical composite structure for mammalian tissue comprising:

a) a reinforcing component prepared from a plurality of fibers, plurality of the fibers manufactured from biocompatible polymer, and

b) a bioabsorbable component comprising a blend of a first and second absorbable polymer, the first absorbable polymer comprising a plurality of linkages selected from the group consisting of glycolic acid ester and lactic acid ester linkages, and mixtures thereof, and the second absorbable polymer comprising a plurality of linkages selected from the group consisting of 1,3-dioxan-2-one; 1,4-dioxan-2-one and ϵ-caprolactone linkages, the first absorbable polymer comprising at least about 50 up to about 90 weight percent of the blend.

29. The structure of embodiment 28 wherein the reinforcing component is manufactured from an absorbable biocompatible polymer.

30. The structure of embodiment 29 wherein the absorbable biocompatible polymer is selected from the group consisting of a homopolymer or copolymer of polyglycolic acid, polylactic acid, polyhydroxy butyrate and blends of the same, and poly(d-lactic acid) blended with poly(l-lactic acid).

31. The structure of embodiment 28 wherein the reinforcing component is manufactured from a nonabsorbable biocompatible polymer.

32. The structure of embodiment 31 wherein the nonabsorbable biocompatible polymer is selected from the group consisting of polyethylene terephthalate, silk, nylon, polypropylene, polyethylene and polyoxymethylene and blends of the same.

33. The structure of embodiment 28, 29, 30, 31 or 32 wherein the first absorbable polymer in the bioabsorbable component is a homopolymer.

34. The structure of embodiment 33 wherein the first absorbable homopolymer in the bioabsorbable component consists essentially of lactic acid ester linkages.

35. The structure of embodiment 28, 29, 30, 31 or 32 wherein the first absorbable polymer in the

bioabsorbable component is a copolymer.

36. The structure of embodiment 35 wherein the second absorbable polymer in the bioabsorbable component comprises a plurality of linkages selected from the group consisting of 1,3-dioxan-2-one and 1,4-dioxan-2-one linkages.

Referring to the embodiments in this Part A, subparagraphs 5, 6, 9, 10 and 14, above, and generally as described in this specification, some polymers have been described as linkages of one or more monomers. Some of these monomers are described as cyclic esters, e.g. 1,4-dioxan-2-one. It is to be understood that any person skilled in the art implicitly knows how to make and how to use these monomers to form the polymer linkages and that, therefore, the description of these linkages by the use of this monomeric nomenclature is adequate.

Referring to the embodiments in this Part A, subparagraphs 1, 6, 10 and 15, above, it is to be clearly understood that the surgical repair and fracture fixation devices include, but are not limited to, those embodiments described in this Part A, subparagraphs 16 to 18, above. Thus, other devices, e.g. a bone pin, bone rod, bone screw, trocar, prosthetic tubular article, and similar or related molded or extruded devices, are within the scope of this invention.

Referring to this Part A, subparagraphs 19 and 28, above, the plurality of fibers in the reinforcing component can be matted, chopped, woven, knitted, unidirectional or a fiber tow. The plurality of fibers can also be composed of laminated plies wherein each ply consists of continuous, unidirectional fibers, woven fabric or knitted fabric and the direction of fibers between adjacent plies need not be the same.

Referring, generally, to this Part A, subparagraphs 19 to 36, above, in the fabrication of the composite structure, it is to be understood that the melting point of the bioabsorbable component must be less than the melting point of the reinforcing component. See also, generally, Example 12.

Referring to the embodiments in this Part A, subparagraphs 20 and 29, above, it is to be understood that other absorbable polymers can be used beside those described in this Part A, subparagraphs 21 and 30, above, respectively. Other absorbable polymers include those described in the "Part A Description", above, subparagraphs 1A and 2A, which description is not exclusive.

The inventions are further described in the following examples:

Example 1

L-Lactide-Trimethylene Carbonate Block Copolymer

Polymerization grade l,3-dioxan-2-one (trimethylene carbonate, hereafter abbreviated TMC) (97.5g, 0.995 mole), diethylene glycol (hereafter abbreviated DEG) (4.20×10^{-2}g, 4.0×10^{-4} mole), and Dabco T-9 catalyst (a stannous 2-ethylhexanoate catalyst formulation sold by Air Products, Inc., USA, hereafter abbreviated T-9) (1.35×10^{-2}g, 3.3×10^{-5} moles) were combined in a stirred reactor at 182°C. The temperature was raised to 188°C and the mixture was stirred for l l/2 hours at this temperature. Polymerization grade l-lactide (52.5g, 0.364 mole) was added and the temperature was increased to 200°C. After 45 minutes, the polymer was discharged from the reactor and allowed to solidify.

The resulting polymer had an inherent viscosity (hereafter abbreviated IV) of 0.89 dL/g (0.5g/dL conc. in $CHCl_3$). The convention to be used to define copolymer composition in this and subsequent examples is "mole percent lactide." This refers to the content of units in the copolymer which would be formed by incorporation of a certain mole percent of lactide monomer into the copolymer. The composition of this copolymer was found to be 20.7 mole percent l-lactide by ^{1}H NMR.

The polymer was dissolved in methylene chloride (5 g/dL) and a film of about 0.003 inch thickness was cast. The resulting material was found to be rubbery at room temperature.

Example 2

L-Lactide-Trimethylene Carbonate Block Copolymer

Polymerization grade TMC (97.5g, 0.995 mole), DEG (4.20×10^{-2}g, 4.0×10^{-4} mole), and T-9 catalyst (1.35×10^{-2}g, 3.3×10^{-5} moles) were combined in a stirred reactor at 180°C and stirred at 40 RPM for l hour and 20 minutes. Polymerization grade l-lactide (52.5g, 0.364 mole) was added and the temperature was increased to 200°C. After l hour, the polymer was discharged from the reactor and allowed to solidify. The solid polymer was then devolatilized under reduced pressure at 25°C to remove residual monomer.

The resulting copolymer had an inherent viscosity of 0.64 dL/g (0.5 g/dL conc. in $CHCl_3$). The composition was found to be 25.7 mole percent l-lactide by ^{1}H NMR.

The polymer was dissolved in methylene chloride (5 g/dL) and a film of about 0.003 inch thickness was cast. The resulting material was found to be rubbery at room temperature.

Example 3

L-Lactide-Trimethylene Carbonate Block Copolymer

Polymerization grade TMC (64.99g, 0.637 mole), DEG (1.83×10^{-2}g, 1.73×10^{-4} mole), and T-9 catalyst (8.0×10^{-3}g, 2.0×10^{-5} moles) were combined in a stirred reactor at 180°C and stirred at 40 RPM for 35 minutes. Polymerization grade l-lactide (154.29g, 1.07 mole) was added and the temperature was increased to 190°C. After 4 hours, the polymer was discharged from the reactor and allowed to solidify.

The resulting copolymer had an inherent viscosity of 1.01 dL/g (0.5 g/dL conc. in $CHCl_3$). The composition was found to be 62.6 mole percent l-lactide by ^1H NMR.

The plaque to be used for test specimen preparation was formed using a heated hydraulic press. At a press temperature of 200°C, about 23 grams of dry polymer granules were pressed in a 4 1/4 inch by 4 l/4 inch by 1/16 inch steel frame between Teflon™ (DuPont Co., DE, USA) coated release liner fabric at 500 pounds of pressure for 4 minutes followed by a pressure increase to 5000 pounds for 4 minutes. The hot plaques were cooled between chilled aluminum plates. The plaques were removed from the frame and annealed in the press at 130°C for 15 minutes at about 250 pounds (14 psi) pressure.

This material was found to undergo ductile deformation through crazing when bent at room temperature.

Example 4

L-Lactide-Trimethylene Carbonate Block Copolymer

Polymerization grade TMC (64.99g, 0.637 mole), DEG (1.83×10^{-2}g, 1.73×10^{-4} mole), and T-9 catalyst (2.06×10^{-2} moles) were combined in a stirred reactor at 180°C and stirred at 40 RPM for 35 minutes. Polymerization grade l-lactide (154.29g, 1.07 mole) was added and the temperature was increased to 190°C. After I hour and 45 minutes, the polymer was discharged from the reactor and allowed to solidify. The polymer was ground cryogenically and dried in vacuum at 105°C for 18 hours.

The resulting copolymer had an inherent viscosity of 1.44 dL/g (0.5 g/dL conc. in $CHCl_3$). The composition was found to be 60.5 mole percent l-lactide by ^1H NMR.

A plaque to be used for test specimen preparation was formed according to Example 3.

This material was found to undergo ductile deformation through crazing when bent at room temperature.

Example 5

L-Lactide-Trimethylene Carbonate Block Copolymer

Polymerization grade TMC (45.94g, 0.450 mole), DEG (1.59×10^{-2}g, 1.49×10^{-4} mole), and T-9 catalyst (1.81×10^{-2}g, 4.48×10^{-5} moles) were combined in a stirred reactor at 180°C and stirred at 40 RPM for 30 minutes. Polymerization grade l-lactide (151.35g, 1.07 mole) was added and the temperature was increased to 195°C. After 2 hours, the polymer was discharged from the reactor and allowed to solidify. The solid polymer was ground cryogenically and was then devolatilized under reduced pressure at 105°C to remove residual monomer.

The resulting copolymer had an inherent viscosity of 1.49 dL/g (0.5 g/dL conc in $CHCl_3$). The composition was found to be 68.3 mole percent l-lactide by ^1H NMR.

A plaque to be used for test specimen preparation was formed according to Example 3.

The material was found to undergo ductile deformation through crazing when bent at room temperature.

Example 6

Dl-Lactide-Trimethylene Carbonate Block Copolymer

Polymerization grade TMC (33.2g, 0.325 mole), DEG (1.72×10^{-2}g, 1.62×10^{-4} mole), and T-9 catalyst (7.6×10^{-3}g, 1.87×10^{-5} moles) were combined in a stirred reactor at 180°C and stirred at 40 RPM for 35 minutes. Polymerization grade dl-lactide (186.8g, l.296 mole) was added and the temperature was increased to 195°C. After 3 hours and 40 minutes the polymer was discharged from the reactor and allowed to

solidify. The solid polymer was ground cryogenically and was then devolatilized under reduced pressure at 25°C for 18 hours to remove residual monomer.

The resulting copolymer had an inherent viscosity of 1.05 dL/g (0.5 g/dL cono. in $CHCl_3$). The composition was found to be 78.6 mole percent dl-lactide by ^1H NMR.

A plaque to be used for test specimen preparation was formed according to Example 3.

This material was found to undergo ductile deformation through crazing when bent at room temperature.

Example 7

L-Lactide-Trimethylene Carbonate Block Copolymer

Polymerization grade TMC (33.2g, 0.325 mole), DEG ($1{,}72x10^{-2}$g, $1.62x10^{-4}$ mole), and T-9 catalyst ($7.6x10^{-3}$g, $1.87x10^{-5}$ moles) were combined in a stirred reactor at 180°C and stirred at 40 RPM for 35 minutes. Polymerization grade l-lactide (186.8g, 1.296 mole) was added and the temperature was increased to 195°C. After 3 hours and 40 minutes, the polymer was discharged from the reactor and allowed to solidify. The solid polymer was ground cryogenically and was then devolatilized under reduced pressure at 150°C for 18 hours to remove residual monomer.

The resulting copolymer had an inherent viscosity of l.56 dL/g (0.5 g/dL conc. in $CHCl_3$). The composition was found to be 79.1 mole percent l-lactide by ^1H NMR.

A plaque to be used for test specimen preparation was formed according to Example 3.

This material was found to undergo ductile deformation through crazing when bent at room temperature.

Example 8

L-Lactide-Trimethylene Carbonate Block Copolymer

Polymerization grade TMC (16.1g, 0.158 mole), DEG ($1.67x10^{-2}$g, $1.57x10^{-4}$ mole), and T-9 catalyst ($6.37x10^{-3}$g, $1.57x10^{-5}$ moles) were combined in a stirred reactor at 180°C and stirred at 40 RPM for 27 minutes. Polymerization grade l-lactide (203.9g l.415 mole) was added and the temperature was increased to 195°C. After 6 hours, the polymer was discharged from the reactor and allowed to solidify. The solid polymer was ground cryogenically and was then devolatilized under reduced pressure at 100°C for 18 hours to remove residual monomer.

The resulting copolymer had an inherent viscosity of 1.41 dL/g (0.5 g/dL conc. in $CHCl_3$). The composition was found to be 89.6 mole percent l-lactide by ^1H NMR.

A plaque to be used for test specimen preparation was formed according to Example 3.

This material was found to undergo a small amount of ductile deformation and crazing before breaking when bent at room temperature.

Example 9

L-Lactide-Trimethylene Carbonate Block Copolymer

Polymerization grade TMC (7.66g, 0.075 mole), DEG ($1.69x10^{-2}$g, $1.59x10^{-4}$ mole), and T-9 catalyst ($1.82x10^{-2}$g, $4.45x10^{-5}$ moles) were combined in a stirred reactor at 180°C and stirred at 40 RPM for 21 minutes. Polymerization grade l-lactide (205.34g, l.425 mole) was added and the temperature was increased to 195°C. After 3 hours and 40 minutes, the polymer was discharged from the reactor and allowed to solidify. The solid polymer was ground cryogenically and was then devolatilized under reduced pressure at 100°C for 18 hours to remove residual monomer.

The resulting copolymer had an inherent viscosity of 1.65 dL/g (0.5 g/dL conc. in $CHCl_3$). The composition was found to be 95.3 mole percent l-lactide by ^1H NMR.

A plaque to be used for test specimen preparation was formed according to Example 3.

This material was not found to undergo ductile deformation when bent at room temperature.

Example 10

Thermal Analysis Of Lactide-TMC Copolymers

Samples of copolymers from Examples 3 to 9 were analyzed by differential scanning calorimetry (DSC).

Scanning conditions were from -40°C to 200°C at 20°C minimum under nitrogen. Those copolymers which formed two amorphous phases are identified by two glass transition temperatures (Tg(1) and Tg(2)). All samples except Example 5, which was made using dl-lactide, also had a crystalline phase characterized by the melting point (Tm) and the enthalpy of fusion (ΔHf). The results of this analysis are shown in Table 1.

Table 1

Polymer From Example	Mole % 1-Lac	Tg(1) (°C)	Tg(2) (°C)	Tm (°C)	ΔHf (cal/g)
3	62.5	-8.8	55.8	167.6	7.28
4	60.5	-12.5	57.8	171.4	8.76
5	68.3	-10.3	57.3	171.1	8.86
6	78.8 (dl)	-4.1	49.4	--	--
7	79.1	-12.5	59.4	172.7	11.63
8	89.6	--	60.3	175.0	11.85
9	95.3	--	65.8	174.8	12.12

Example 11

Mechanical Testing of Lactide-TMC Copolymers

Plaques made in Examples 4 through 8 were cut into specimens for testing according to ASTM methods D638 (tensile) and D790 (flexural). The results of this testing are included in Table 2. For the tensile tests, five replicates were used, and the mean values are reported in Table 2. The flexural values reported in Table 2 are the means for four replicates.

Table 2

Tensile Results (ASTM D638)

Sample From Example	Mole % l-lac	Modulus (10^3 psi)	At Break Strength (10^3 psi)	At Break Strain (10^1 %)	At Yield Strength (10^3 psi)	At Yield Strain (%)
4	60.5	240	4.6	10	4.9	3.9
5	68.3	310	5.7	12	6.3	3.7
6	78.8 (dl)	400	4.4	2.0	6.6	2.4
7	79.1	400	6.3	0.5	7.6	2.7
8	89.6	480	7.3	0.43	8.7	2.4
9	95.3	520	8.1	0.18	--	--

Flexural Results (ASTM D790)

Sample From Example	Mole % l-lac	Modulus (10^3 psi)	Strength (10^3 psi)	Strain (10^1 %)	Strength (10^3 psi)	Strain (%)
4	60.5	260	7.5	12	9.0	5.5
5	68.3	340	9.4	12	11.4	5.1
6	78.8 (dl)	390	7.7	11	10.4	3.8
7	79.1	480	11.8	12	14.7	4.8
8	89.6	620	17.2	6.15	18.1	4.8
9	95.3	710	14.5	2.16	--	--

The flexural and tensile results indicate that the copolymers with 60 to 90 percent lactide form materials which will undergo ductile deformation through crazing. For a bone plate application, it is considered desirable to have the highest modulus and yield strength, while maintaining ductility. The preferred composition for the bone plate application, in the case of lactide-TMC block copolymers, would, therefore, be 80 to 90 percent lactide. Above 90 percent lactide, the sample loses ductility, and below 80 percent

lactide, the modulus and yield strength continue to decrease without any advantage in ductility as measured by strain at break in flexure.

Example 12

Composite Fabrication

A composite was fabricated in the following manner. Poly(glycolic acid) (PGA) fiber (100 g/denier) was wound around a 7 3/4" square stainless steel plate. The fiber covered both sides of the plate over a section measuring 3" x 7 3/4" with the long dimension aligned with the fiber. The weight of fiber used for this operation was 12.0 g.

A 10 g/dL solution of the polymer of Example 7 was prepared in methylene chloride. Polymer was then brushed onto the fiber and air dried. This was repeated several times. The material was then consolidated in a heated press at 170°C and cooled to room temperature. This allowed for the fiber to be cut and the two halves removed from front and back side of the plate. Additional polymer solution was applied to the two sections. This was continued until a total of 19.0 g of polymer was added to the fiber. The two halves were then vacuum pressed to a thickness of 1/16" at a temperature of 170°C. The composite was removed from the press and annealed at 110°C in an air oven for twenty minutes. The final weight fraction of PGA in the composite was 39%.

The plate was cut into 1/2" X 2 1/2" tensile specimens and tested according to ASTM D638 (Amer. Soc. of Testing Materials, PA, USA). The tensile modulus was 0.99 X 10^6 psi and the tensile strength was 37.0 X 10^3 psi.

Two tensile specimens were strained in flexure (ASTM D790) to 5% in an Instron test machine (Instron Corp., MA, USA). When the load was relieved, the specimens were permanently deformed to approximately 2% strain. Flexural modulus was 1.27 X 10^6 psi and flexural stress at 5% strain was 21.6 X 10^3 psi.

Part B

The prior art discloses certain nonabsorbable materials that contain 0.05 to 20 percent polytetrafluoroethylene ("PTFE") microfibrous particles. The PTFE is described as useful as an additive to improve viscosity and melt elasticity of certain thermoplastics. The prior art also discloses a method for making a molding composition containing 10 to 20 percent PTFE with a thermoplastic polymer. The composition was found to provide improved impact strength. The prior art also discloses a composition of polyethylene terephthalate with 0.1 to 2.0 percent by weight of a PTFE emulsion incorporated therein. The PTFE additive is said to improve the processability. It also discloses that PTFE also unexpectedly increases the ultimate elongation of the final compositions. No mention is made in any of the prior art of the usefulness of the materials as deformable articles. No mention of their usefulness in medical products is made. Also, no mention of their usefulness with absorbable polymers is made. In summary, none of the prior art mentions the usefulness as medical devices of absorbable materials combined with PTFE, which can be permanently deformed at room temperature through crazing.

The following embodiments summarize the Part B inventions:

1. An article of manufacture comprising a deformable surgical repair device, the deformable surgical repair device manufactured from an absorbable material, the absorbable material having a polymer comprising linkages selected from the group consisting of glycolic acid ester, lactic acid ester, 1,3-dioxan -2-one and l,4-dioxan-2-one linkages, the surgical repair device further manufactured from a nonabsorbable material.

2. The article of embodiment 1 wherein the nonabsorbable material comprises a polymer prepared from a fluorinated hydrocarbon.

3. The article of embodiment 2 wherein the absorbable material comprises a homopolymer.

4. The article of embodiment 3 wherein the absorbable material comprises a homopolymer consisting essentially of glycolic acid ester linkages.

5. The article of embodiment 1, 2 or 3 wherein the absorbable material comprises a homopolymer consisting essentially of lactic acid ester linkages.

6. The article of embodiment 1 or 2 wherein the absorbable material comprises a copolymer comprising glycolic acid ester and lactic acid ester linkages.

7. An article of manufacture comprising a deformable tissue repair device, the deformable tissue repair device manufactured from an absorbable material, the absorbable material having a first homopolymer consisting essentially of linkages selected from the group consisting of glycolic acid ester, lactic acid

ester and l,4-dioxan-2-one linkages blended with a second copolymer comprising at least two different linkages selected from the group consisting of glycolic acid ester, lactic acid ester, l,3-dioxan-2-one, l,4-dioxan-2-one and ϵ-caprolactone linkages, the tissue repair device further manufactured from a nonabsorbable material.

8. The article of embodiment 7 wherein the non-absorbable material comprises a polymer prepared from a fluorinated hydrocarbon.

9. The article of embodiment 8 wherein the first homopolymer consists essentially of glycolic acid ester linkages.

10. The article of embodiment 7 or 8 wherein the first homopolymer consists essentially of lactic acid ester linkages.

11. The article of embodiment 9 wherein the second copolymer comprises glycolic acid ester and trimethylene carbonate linkages.

12. The article of embodiment 7, 8, 9 or 11 wherein the second copolymer comprises glycolic acid ester and lactic acid ester linkages.

13. The article of embodiment 2, 3, 4, 8, 9 or 11 wherein the nonabsorbable material is polytetrafluoroethylene.

14. An article of manufacture comprising a deformable surgical repair device, the deformable surgical repair device manufactured from an absorbable material, the absorbable material having a first homopolymer comprising linkages selected from the group consisting of glycolic acid ester, lactic acid ester and l,4-dioxan-2-one linkages blended with a second copolymer comprising at least two different linkages selected from the group consisting of glycolic acid ester, lactic acid ester, 1,3-dioxan-2-one, l,4-dioxan-2-one and ϵ-caprolactone linkages, the deformable surgical repair device further manufactured from a nonabsorbable material, the nonabsorbable material comprising a polymer selected from the group consisting of polytetrafluoroethylene and a fluorinated ethylene-propylene copolymer, the nonabsorbable material comprising more than about 1/100th of one percent to less than about one percent by weight of the device.

15. The article of embodiment 14 wherein the first homopolymer consists essentially of glycolic acid ester linkages.

16. The article of embodiment 14 wherein the first homopolymer consists essentially of lactic acid ester linkages.

17. The article of embodiment 15 wherein the second copolymer comprises glycolic acid ester and trimethylene carbonate linkages.

18. The article of embodiment 14, 15, 16 or 17 wherein the nonabsorbable material is polytetrafluoroethylene.

19. The article of embodiment 18 wherein the nonabsorbable material comprises more than about 1/50th to less than about one-half of one percent by weight of the device.

20. The article of embodiment 19 wherein the nonabsorbable material comprises about 1/10th of one percent.

21. The article of embodiment 2, 3, 4, 8, 9, 11, 14, 15 or 17 wherein the nonabsorbable material is micropulverized.

22. The article of embodiment 2, 3, 4, 8, 9, 11, 14, 15 or 17 wherein the nonabsorbable material is in microfibrillar form.

23. The article of embodiment 2, 3, 4, 8, 9 11, 14, 15 or 17 wherein the deformable repair device is a fracture fixation device.

24. The article of embodiment 23 wherein the fracture fixation device is a bone plate.

25. The article of embodiment 2, 3, 4, 8, 9, 11, 14, 15 or 17 wherein the deformable repair device is a clip.

26. The article of embodiment 2, 3, 4, 8, 9, 11, 14, 15 or 17 wherein the deformable repair device is a staple.

Referring to the embodiments in this Part B, subparagraphs 1 and 7 above, it is to be clearly understood that the nonabsorbable material is limited to those nonabsorbable compositions of matter which promote crazing. The mechanics of crazing of a polymeric material is well known in the prior art, although it is to be noted that the prior art almost always teaches that a crazing mechanism is not an advantage. Therefore, the invention described in this application teaches away from the known prior art.

Referring to the embodiments in this Part B, subparagraphs 1, 7 and 14, above, and generally as described in this specification, some polymers have been described as linkages of one or more monomers. Some of these monomers are described as cyclic esters, e.g. 1,4-dioxan-2-one. It is to be understood that any person skilled in the art implicitly knows how to make and how to use these monomers to form the

polymer linkages and that therefore the description of these linkages by the use of this monomeric nomenclature is adequate.

Referring to the embodiments in this Part B, subparagraphs 1, 7, 14 and 23, above, it is to be clearly understood that the surgical repair, tissue repair and fracture fixation devices include, but are not limited to, those embodiments described in this Part B, subparagraphs 24 to 26 above. Thus, other devices, e.g. a bone pin, bone rod, bone screw, trocar, prosthetic tubular article and similar or related molded or extruded devices, are within the scope of this invention.

Referring to the embodiments in this Part B, subparagraphs 21 and 22, above, a description of a micropulverized or microfibrillar fluorinated hydrocarbon polymer, and specifically polytetrafluoroethylene is disclosed in the prior art.

Part B DESCRIPTION

This invention relates to partially absorbable polymeric materials possessing an enhanced ability for permanent deformation at room temperature through a crazing mechanism. This invention also relates to the use of these materials in medical device applications that require the material to be reshapable. Applications where these materials may be useful include the following:

1. Maxillofacial bone fixation plates.
2. Bone screws or other fastening devices.
3. Surgical clips and staples.

Although not specifically exemplified, it is recognized that a number of materials could be envisioned which could possess similar properties to the exemplified compositions. To have similar properties, it is necessary that the material have a continuous "hard" phase and a "soft" phase. The soft phase in this invention is PTFE. The PTFE has been compounded with a normally rigid absorbable polymer, which forms the hard phase, by applying shear to the molten polymer in the presence of PTFE powder. The following is a list of alternative materials which are included in this invention:

Hard phase forming absorbable polymers

1. Poly(1-lactide), poly(d-lactide) or poly(meso-lactide)
2. Copolymers of 1-lactide and d-lactide
3. Polyglycolide
4. Lactide-glycolide copolymers
5. Other polymers or copolymers with glass transition temperatures above room temperature.

The selection of a preferred material will depend on the desired physical properties of the final article. The preferred material will also be determined by the desired in vivo degradation and absorption rates. Several variables can be adjusted to obtain the desired properties. Absorption rate is known to be affected by composition and crystallinity -- for example, a hard phase of poly(1-lactide) would provide a slow degradation rate due to its hydrophobic, crystalline nature, whereas a copolymer of glycolide and dl-lactide in equal amounts would provide a fast degradation rate due to its more hydrophilic, noncrystalline nature. If increased stiffness or strength is required, a fiber or fabric reinforcement can be added to make a composite structure. Further improvement of the composite properties can be made by manipulating the location of the reinforcement within the composite -- for example, if the reinforcement is placed in the center plane of a laminated structure, the composite would be expected to be stiffer in tension (forces applied parallel to the plane) than in flexion (forces applied normal to the plane), allowing reshaping by bending.

The inventions are described in the following examples:

Example 13

Polyglycolide Containing 0.1% Teflon

Polyglycolide (63g) obtained from Davis & Geck, Wayne, NJ, USA was charged to the mixing head of an Electronic Plasti-corder manufactured by C. W. Brabender Instruments, Inc., NJ, USA. The polymer was heated to its melt temperature and mixed at 40 rpm while 0.063g of Teflon™ DLX 6000 powder (DuPont, DE, USA) was added. The mixing rate was increased to 75 rpm for two minutes and the molten mixture was removed from the mixing head and allowed to cool to room temperature.

Example 14

Polyglycolide Containing I.0% Teflon

The procedure of Example 13 was used to prepare a blend of 0.63g of Teflon™ DLX 6000 powder in 63g of polyglycolide.

Example 15

Polyglycolide/Poly(Glycolide-co-trimethylene carbonate) (50/50 Weight Ratio) Containing 0.1% Teflon

The procedure of Example 13 was used to mix 0.1% by weight of Teflon™ DLX 6000 powder into a 50/50 weight ratio blend of polyglycolide and poly(glycolide-co-trimethylene carbonate). The 50/50 weight ratio blend was obtained from Davis & Geck, Wayne, NJ, USA.

Example 16

Polyglycolide/Poly(Glycolide-co-trimethylene carbonate) (75/25 Weight Ratio) Containing 0.1% Teflon

The procedure of Example 13 was used to mix 0.1% by weight of Teflon™ DLX 6000 powder into a 75/25 weight ratio blend of polyglycolide and poly(glycolide-co-trimethylene carbonate).

Example 17

Molded Plaques

The polymer-Teflon™ blends of Examples 13 to 16 were molded into 1/16" thick plaques by heating each of the blends at a temperature of 230°C. and a pressure of 555 psi for one (I) minute between two Teflon™ coated aluminum plates separated by a I/16" thick spacer.

The plaques were allowed to cool to room temperature and were then cut into 1/4" wide strips for manual testing of how readily the strips could be deformed at ambient temperature. The results of the manual testing are summarized in Table I.

Example 18

Control

Control strips were fabricated according to the procedure of Example 17, above, from polyglycolide that did not contain Teflon™ particles. The control strips were then manually tested as described above. The results of the manual testing of the control strips are summarized in Table 3.

TABLE 3

Cold Formable Absorbable Polymers

Example	Polymer	Teflon Wt.%	Maximum Bend, Deg.	Comments
1	PGA[1]	1.0	90-100	Broke when bent more than 90-100°
2	PGA	0.1	180	Partial rebound[3] (about 25%)
3	PGA/p(Gly/TMC)[2] Blend 50/50 Wt. Ratio	0.1	180	Rebounds (more than 50%)
4	PGA/p(Gly/TMC) Blend 75/25 Wt. Ratio	0.1	180	Rebounds (more than 50%)
6	PGA control	0	small deformation	Broke

(1) PGA: Polyglycolide

(2) p(Gly/TMC): Poly(glycolide-co-trimethylene carbonate), which is described in U.S. patent 4,429,080. This patent is incorporated herein by reference.

(3) On release of the force required to effect a 180° blend, some of the folded strips opened.

Claims

1. A deformable surgical repair device manufactured from either an absorbable copolymer comprising a plurality of first and second linkages or an absorbable blend of a first and second polymer, the

copolymer first linkages and the first polymer in the blend selected from the group consisting of glycolic acid ester and lactic acid ester linkages, and mixtures thereof; and the copolymer second linkages and the second polymer in the blend selected from the group consisting of 1,3-dioxan-2-one; 1,4-dioxan-2-one and ε-caprolactone linkages, the plurality of first linkages or the first polymer comprising at least about 50 up to about 90 mole percent of the respective copolymer or blend.

2. The device of claim 1 wherein the absorbable copolymer is a block or graft copolymer.

3. The device of claim 2 wherein the absorbable copolymer is a block copolymer, and said plurality of first linkages comprises lactic acid ester linkages and second linkages comprises 1,3-dioxan-2-one linkages.

4. The device of claim 1 wherein said first polymer in the absorbable blend is a homopolymer consisting essentially of lactic acid ester linkages.

5. The device of claim 1 in combination with a reinforcing component prepared from a plurality of fibers manufactured from a biocompatible polymer.

6. The device of claim 5 wherein the reinforcing component is manufactured from either an absorbable biocompatible polymer selected from the group consisting of a homopolymer or copolymer of polyglycolic acid, polylactic acid, polyhydroxy butyrate and blends of the same, and poly(d-lactic acid) blended with poly(1-lactic acid), or a nonabsorbable bicompatible polymer selected from the group consisting of polyethylene terephthalate, silk, nylon, polypropylene, polyethylene and polyoxymethylene and blends of the same.

7. The device of claim 1 further manufactured from a nonabsorbable material.

8. The device of claim 7 having a first absorbable homopolymer blended with a second absorbable copolymer, and the nonabsorbable material comprising a polymer prepared from a fluorinated hydrocarbon.

9. The device of claim 8 wherein the first homopolymer consists essentially of glycolic acid ester linkages.

10. The device of claim 8 wherein the second copolymer comprises at least two different linkages selected from the group consisting of glycolic acid ester, lactic acid ester, 1,3-dioxan-2-one, 1,4-dioxan-2-one and e-caprolactone linkages, and the fluorinated hydrocarbon polymer is selected from the group consisting of polytetrafluoroethylene and a fluorinated ethylene-propylene copolymer, the nonabsorbable material comprising more than about 1/100th of one percent to less than about one percent by weight of said device.

11. The device of claim 10 wherein the second copolymer comprises glycolic acid ester and trimethylene carbonate linkages and said nonabsorbable material is polytetrafluoroethylene.

12. The device of claim 10 wherein said non-absorbable material comprises more than about 1/50th to less than about one-half of one percent by weight of said device and is in a micropulverized or microfibrillar form.

13. The device of claims 1 to 12 as a clip.

14. The device of claims 1 to 12 as a staple.

15. The device of claims 1 to 12 as a fracture fixation device.

16. The device of claim 15 wherein the fracture fixation device is selected from the group consisting of a bone plate, bone pin, bone rod and bone screw.